Supplemental Methods:

Human MSC isolation from bone marrow, adipose tissue and umbilical cord

Human MSCs were isolated from bone marrow, adipose tissue and umbilical cord from individuals upon consenting and institutional review board approval. Harvested bone marrow was separated by Ficoll density gradient and plated on α-MEM culture medium containing 15% human platelet lysate and 100 U/ml penicillin/streptomycin (200,000 cell/cm^2). Umbilical cord and adipose tissues were minced to less than $1CM^2$ cubes and left in a medium containing 15% human platelet lysate and 100 U/ml penicillin/streptomycin. Once MSC colonies appeared, cells were trypsinized, seeded and allowed to expand as passage 0. Subsequently, MSCs were passaged weekly and replated at a seeding density of 1000 cells/cm^2. All assays were performed using MSC between passage 2 and 6.

MSC phenotype

Live or heat inactivated (56 degree Celsius for 30 minutes, Cells were counted prior to heat inactivation) MSCs were subjected to flow cytometry with the antibodies CD105PE, CD44PE, CD73PE, CD90APC CD45PE, appropriate isotype controls, 7AAD (BD Biosciences, St Jose, CA). Histogram analysis for the marker expression was performed with Flow Jo software.

MSC and PBMC coculture

Live or heat inactivated MSCs from bone marrow, adipose tissue and umbilical cord (n=2 donors each) were seeded into 96-well plates at a density of 50,000, 25,000, 12,500, 6,250 or 0 cells per well and 100,000 human peripheral blood mononuclear cells (PBMCs) added to each well with 1000 ng/ml staphylococcal enterotoxin B (SEB) (Toxin Technology, Sarasota, FL). MSCs at a similar density without PBMCs were used a reference control. For kinetic analysis assay, MSCs from bone marrow were added on to 384 well plates with the density of 25000, 20000, 15000, 10000, 5000, 2500, 1250 and 0. Subsequently 25000 PBMCs were added to each well with 1000ng/ml SEB. Four days post culture, a Ki67 flow cytometric proliferation assay was performed, according to the manufacturer instructions with CD3-APC-Cy7 and Ki67-PE antibodies (BD Biosciences, San Jose, CA).

Phosflow assays

Supernatants from co-culture of MSCs and/or PBMCs were collected after 4 days or kinetically on days 1, 2 3, 4, and stored at -80°C. Stored supernatants were thawed and centrifuged at 500xg for 3 min to eliminate cell debris and equilibrated to in the 37C for an hour. These supernatants were used for the stimulation of the MSCs for 15 minutes and fixed with BD cytofix buffer for 10 minutes. Subsequently, cells were permeabilized with BD Phosflow Perm Buffer for 30 minutes and then were subjected to flow cytometry with antibodies Alexa Fluor® 647 Anti-Stat1 (pY701), Alexa Fluor® 647 Anti-Stat3 (pY705), Alexa Fluor® 647 Anti-Stat4 (pY693), Alexa Fluor® 647 Anti-Stat5 (pY694), Alexa Fluor® 647 Anti-Stat6 (pY641) (BD Biosciences, San Jose, CA). Results were analyzed in Flow Jo software.

Statistical methods

Correlation between secretome and T-cell proliferation were performed using linear regression analyses to obtain R^2 and P values and Area under curve (AUC) values were obbtained in GraphPad Prism 5.0 software.